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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,071	01/08/2001	Karl Tryggvason	TRV 20014 P	6472

7590 07/30/2002

Richard J. Minnich
7th Floor
1100 Superior Ave.
Cleveland, OH 44114

EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	12

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/756,071	TRYGGVASON ET AL.	
	Examin r	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in Paper No. 11 is acknowledged. Claims 4-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim.

Preliminary Amendment

2. The amendment filed April 11, 2002 has been entered. Claim 1 has been amended. Claims 1-3 are under consideration in office action.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The benefit of the earlier filing date under 35 U.S.C. 120 of the parent application Serial No. 08/317,450, 08/800,593 and 60/175,005 has been denied for claims 1-3 for the instant application. The claims in the instant continuation-in-part application recite a feature, i.e., a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain antibodies to inhibit the gamma2chain biological activity of said invasive carcinomas which was not disclosed or adequately supported by a proper disclosure under 35 U.S.C. 112 in the parent applications. This feature has been first introduced in the instant continuation-in-part application and thus such claims are entitled only to the filing date of the instant

application; In re Von Lagenhoven , 458 F.2d 132, 136, 173 USPQ 426, 429 (CCPA 1972) and Chromalloy American Corp. v. Alloy Surfaces Co ., Inc ., 339 F. Supp. 859, 874, 173 USPQ 295, 306 (D. Del. 1972).

Drawings

4. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: 2A', 2B', 2E', 2F' and 2G' in figure 2; figures 3A and 3A' are described however the figures are named 3A-1 in the actual figure; and there is no description and corresponding SEQ ID Number descriptions of figures 4C and 4D. A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas.

However said method fails to meet the written description provision of 35 UCS 112, first paragraph. Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification only discloses antibodies against gamma2 domain III, but not domain I/II inhibit cell migration. There is no teaching of polyclonal or monoclonal antibodies inhibiting gamma2 chain biological activity of the invasive carcinoma or the intervention of the carcinomas with surrounding tissues using any anti-gamma2 chain antibody. A method for inhibiting cell migration is not equivalent to a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using

anti-gamma2 chain antibodies to inhibit the gamma2chain biological activity of said invasive carcinomas.

A skilled artisan cannot envision the detailed steps of the claimed method since the specification has not defined what the method steps are: what type of patient the method would work in i.e., mice or humans; how, where and at what dosage the antibody is administered; what type of biological activity is inhibited; or the specific type of anti-gamma2 chain antibody. There are no examples of using the method for intervention of gamma2 chain interactions of invasive carcinomas. There are no in vitro or in vivo test which could correspond to said method. There is no teaching of either polyclonal or monoclonal antibodies that inhibit the gamma2 chain biological activity of invasive carcinomas. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The amino acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The claims fail to recite the precise definition of the antibodies used or what type of biological activity is being inhibited. Currently the method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas is insufficient to support the claims as provided by the Interim Written

Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The specification does not provide a clear protocol by which the method for intervention could be practiced at the time the invention was made. In view of the lack of evidence in the specification as filed, it is apparent that one skilled in the art would recognize that applicants were not in possession, at the time of filing the instant application, of a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain polyclonal or monoclonal antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas. The specification does not teach a representative example from which the method is based upon. As previously stated, applicants have not shown a method for intervention which is sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Thus a skilled artisan cannot envision said method and therefore conception cannot be achieved until reduction to practice has occurred. Therefore, the claims lack written description of a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain polyclonal or monoclonal antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas. In view of the lack of written description of the claims, the full breadth of the claims fail to meet the written description provision of 35 USC 112, first paragraph.

6. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas. The specification lacks any description of antibodies inhibiting gamma2 chain biological activity of the invasive carcinoma; the intervention of the carcinomas with surrounding tissues using any anti-gamma2 chain antibody. The specification fails to teach that the method for inhibiting cell migration is equivalent to a method for intervention of gamma2 chain interactions of invasive carcinomas with surrounding tissues by using anti-gamma2 chain antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas, thus there are no examples of the claimed method. There is no teaching of what type of patient the method would work; other methods in the specification transgenic mice however, it should be noted that the mice are not an acceptable human model. There is no teaching of a mode of administration such where and at what dosage the antibody is administered. Moreover, the method does not even state how the anti-gamma2 chain polyclonal or monoclonal antibody is used. There is no teaching of what type of biological activity is inhibited. The method is not the specific type of anti-gamma2 chain antibody, since the specification teaches antibodies drawn to specific domains. There are no in vitro or in vivo examples. There are no working

examples of using the method for intervention of gamma2 chain interactions of invasive carcinomas. None of these consideration have been contemplated in the specification, and in absence of these considerations, there is no assurance that the antibodies would be available in effective doses at the target sites and for the periods of time to affect the interaction of invasive carcinomas with surrounding tissues.

There is no experimentation of such method, as to the quantity of experimentation needed to determine whether to method is enabled. There is no direction or guidance in the specification, and there is a complete lack of working examples. As stated above, the specification does not provide an enabling disclosure supporting the use of the anti-gamma2 chain antibodies to inhibit the gamma2 chain biological activity of the invasive carcinomas. In view of the lack of examples and guidance, the method is unpredictable and would require undue experimentation since a skilled artisan would be required to de novo determine the whether the claimed invention is enabled and the working parameters for said invention. As evidenced by Seaver (Genetic Engineering 14(14): 10 and 21, 1994) selection of a monoclonal antibody as an immunotherapeutic agent is an unpredictable task as the antibody must possess sufficient specificity and a high degree of affinity for its target for use as an immunotherapeutic agent and because these qualities are dependent on the physiology of the particular pathology and the accessibility of the target antigen (column 7, page 10 and column 3 page 21). The specification does not suggest what sort of specificity and affinity would be necessary for the antibodies of the claimed immunotheraphy so that

one skilled in the art would not be able to practice the claimed invention without undue experimentation.

In absence of further guidance from Applicants, the skilled artisan would have to discover what the appropriate antibodies, reagents and method steps would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of the claimed method. The claimed method would not predictably result in an enabled method for intervention. The specification does not provide guidance on how the antibodies can be used to inhibit the gamma2 chain biological activity of invasive carcinomas. No working examples are shown containing the missing information. Without such information, one of skill in the art could not predict a method that would result in the desired method for intervention. Accordingly, one of skill in the art would be required to perform undue experimentation to use the antibodies to inhibit the gamma2 chain biological activity of said invasive carcinomas. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

7. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "biological activity" in claim 1 is a relative term which renders the claim indefinite. The term "biological activity" is not defined by the claim, the specification

does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Thus the metes and bounds of the term cannot be ascertained, i.e., what particular biological activity is inhibited?

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines JH
July 22, 2002

MARK NAVARRO
PRIMARY EXAMINER